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09/500,635	02/09/2000	F. Abel Ponce de Leon	002076-033	2892

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EXAMINER
WILSON, MICHAEL C

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 05/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/500,635	Applicant(s) Ponce De Leon, et al.
	Examiner Michael C. Wilson	Art Unit 1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 24, 2003* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *21-32* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *21-32* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2-24-03, paper number 19, has been entered.

The amendment filed 9-9-02, paper number 16, has been entered. Claims 33-35 have been added. Claims 21-35 are under consideration in the instant application.

Applicant's arguments filed 2-19-02, paper number 12, have been fully considered but they are not persuasive. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

1. The first line of the specification needs updated to indicate 08/905,773 is now US Patent 6,156,569.

Claim Rejections - 35 USC § 112

2. Claims 21-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Culturing PGCs for at least 14 days in the absence of feeder cells and bFGF, SCF, LIF and IGF (claim 21) does not have support in the specification as originally filed. Applicants point to pg 10, line 11, which does not teach culturing the cells in the absence of feeder cells as claimed. Applicants discuss the teachings in the specification but do not teach where the specification taught the method claimed in the absence of feeder cells. None of the citations provided indicate culturing PGCs for fourteen days in the absence of feeder cells. Pg 13, line 20, teaches PGCs were cultured in the absence of feeder cells, but that feeder cells were optional. Pg 21, line 1, teaches feeder cells were used. Pg 27, line 14, teaches feeder cells did not improve the long term culture of PGCs. Pg 28, line 21, teaches culturing PGCs for 25 days or four months but only states the cells were cultured using the four growth factors (pg 29, line 20). From these citations, especially pg 21, line which teaches feeder cells were used, the specification does not describe maintaining PGCs for at least fourteen days in the absence of feeder cells as claimed.

Culturing PGCs in bFGF, SCF, LIF and IGF in the absence of feeder cells and sustaining the culture for 28 days or 4 months (claims 27-28) does not have support in the specification as originally filed.

Introducing a "nucleic acid that encodes a polypeptide and is functionally linked to gene expression regulatory sequences that are operable in an avian cell" into PGCs (claims 29 and 32)

does not have support on pg 17, lines 5-7 and 17-20, which only teaches introducing DNA encoding a polypeptide operably linked to regulatory sequences that function in avian cells.

3. Claims 21-32 remain rejected and claims 33-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for culturing avian PGCs in the presence of LIF, bFGF, SCF and IGF and in the absence of feeder cells, does not reasonably provide enablement for one of skill to determine the conditions essential to maintain cells for 14 days, 28 days or 4 months. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 21 requires culturing avian PGCs in the presence of LIF, bFGF, SCF and IGF and in the absence of feeder cells for at least fourteen days. While the specification states feeder cells did not improve "long term culture" of the PGCs (pg 27, line 14), the specification does not teach the specific conditions required to maintain PGCs for a 14 days, 28 days or 4 months. The specification describes maintaining PGCs for 7 days (pg 22, line 4) and PGC clumps for up to four weeks (pg 22, line 7); however, the specification does not teach this was done in the absence of feeder cells. Overall, the specification does not describe the essential conditions required to maintain PGCs for 14 days, 28 days, or 4 months in the presence of LIF, bFGF, SCF and IGF and in the absence of feeder cells.

Applicants have not argued this rejection.

Claim 29 is directed toward a method of culturing avian PGCs for 14 days and transfecting the PGCs with a nucleic acid sequence. Claim 32 is directed toward a culture of PGCs wherein the PGCs are transfected with DNA. The only disclosed purpose for transfecting PGCs cells is to make a transgenic avian which is used to isolate exogenous proteins from the avian (page 8, line 22) or to change the phenotype of the bird (page 2, line 21). However, Han et al. (Asian-Australasian Journal of Animal Sciences, (1994) Vol. 7, No. 3, pg 427-434) taught transfecting PGCs and using the cells to observe the migration of PGCs through an embryo. Despite the fact that the specification states "no stable transfected cell line has been developed" (pg 30, line 8), given the teachings of Han, it would not have required one of skill undue experimentation to determine how to obtain and use the transfected PGCs claimed for the purpose of observing the migration of PGCs in an embryo as taught by Han.

4. Claims 21-32 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear how the phrase "at least the following growth factors in amounts sufficient to maintain said PGCs for at least fourteen days in tissue culture in the absence of feeder cells" contributes to claim 21. The claim already requires "culturing said PGCs for at least fourteen days in the absence of feeder cells in a culture medium comprising at least the following growth factors...:" LIF, bFGF, SCF and IGF.

The scope of "maintenance" (preamble) and "culturing" (step ii, claim 21) are not commensurate in scope. The phrase "the maintenance" in the preamble should be changed to "culturing".

Claim 22 is grammatically unclear. The limitation should be "wherein said growth factors have minimal concentrations of:..." to be clear.

Claim 23 is grammatically unclear. The limitation should be "wherein said growth factors have a concentration in the range of from about two to one hundred times said minimal concentrations."

Claim 26 does not further limit claim 21 which already requires culturing the PGCs for at least fourteen days.

Claim 29 is grammatically unclear. The limitation should be "transfecting the PGCs cultured for at least fourteen days with a nucleotide sequence encoding a polypeptide functionally linked to gene expression regulatory sequences operable in an avian cell."

The phrase "said culture being free of feeder cells and comprising medium comprising LIF, bFGF, SCF, and IGF" (claims 30 and 32) does not further limit the PGCs produced according to claim 21 which requires the PGCs be cultured in the presence of LIF, bFGF, SCF, and IGF and the absence of feeder cells.

Claim 32 is grammatically unclear. The limitation should be "A culture comprising PGCs cultured for at least fourteen days according to claim 21 comprising a nucleotide sequence

encoding a polypeptide functionally linked to gene expression regulatory sequences operable in an avian cell."

Claim Rejections - 35 USC § 102

5. Claims 21-28, 30 and 31 remain rejected under 35 U.S.C. 102(b) as being anticipated by Pain (7-25-96, Development, Vol. 122, pages 2339-2348, UnCover online at http://uncweb.carl.org/uncover/unchome.html) or in the alternative under 102 (a) as being anticipated by Pain (Aug. 1996, Development, Vol. 122, pages 2339-2348) and supported by Simkiss (1994, MacLean, ed., Animals with novel genes, Transgenic birds, Cambridge Univ. Press, Cambridge England, NY, NY, pages 106-137) for reasons of record.

Pain taught culturing avian blastodermal cells in complete media comprising bFGF, IGF, SCF and LIF in the absence feeder cells for 5 days (pg 2342, Fig. 2D), culturing PGCs for 160 days with bFGF, IGF, SCF and IGF in the presence of feeder cells (pg 2345, col. 2, line 10), and that "the cultures" were maintained with or without feeder cells (page 2341, col. 2, para. 4). Without evidence to the contrary, "the culture" maintained for 160 days was maintained without feeder cells. The PGCs inherently form a monolayer as newly claimed because the culture conditions taught by applicants are indentical to those taught by Pain. The avian blastodermal cells isolated from Stage X embryos of Pain have PGCs as claimed (Simkiss, pg 111, Fig. 4.1, top panel).

Applicants state Pain taken with Simkiss did not teach culturing avian PGCs in vitro in medium containing LIF, bFGF, SCF and IGF-1 for at least 14 days in the absence of feeder cells. This statement is not considered an argument because it is not specific. All the limitations mentioned have been addressed in the rejection. The statement does not specifically state what specific limitation is missing from the references.

Applicants state Pain and other references taught away from the method claimed (pg 7 of response, 6 lines from the bottom). This statement is not considered an argument because applicants do not discuss why Pain taught away from the method.

Applicants describe the teachings of Pain (pg 7, 4 lines from the bottom through pg 8, line 11, of response). Applicants conclude that Pain stated feeder cells strongly promoted AP+ colonies and specifically described culturing CEC for 160 days using feeder cells. Applicants argument is unclear but will be addressed to the greatest extent possible. While Pain taught a preferred method of culturing cells included feeder cells (pg 2345, col. 2, line 10), and maintaining CECs for 160 days using feeder cells (pg 2345, col. 2, line 10), Pain did not teach culturing CEC for 160 days was limited to using feeder cells. Pain also taught "the cultures" were maintained with or without feeder cells (page 2341, col. 2, para. 4). Without evidence to the contrary, "the cultures" maintained without feeder cells includes "the culture" maintained for 160 days.

Claims 30 and 31, directed toward a culture made by the method described above, are anticipated by Pain. The culture described by Pain does not differ from the culture claimed. The

culture of Pain has a combination of PGCs and EG cells. The method used to make the culture as claimed does not alter the structure or function of the culture so as to distinguish it from the culture of Pain. The method does not bear patentable weight in considering the art for claims 30 and 31 because it does not alter the structure or function of the culture.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 21-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pain et al. (7-25-96, Development, Vol. 122, pages 2339-2348, UnCover online at http://uncweb.carl.org/uncover/unchome.html) or Pain et al. (Aug. 1996, Development, Vol. 122, pages 2339-2348) as supported by Simkiss (1994, MacLean, ed., Animals with novel genes, Transgenic birds, Cambridge Univ. Press, Cambridge England, NY, NY, pages 106-137) in view of Han et al. (Asian-Australasian Journal of Animal Sciences, (1994) Vol. 7, No. 3, pg 427-434).

Pain taught culturing PGCs in complete media comprising bFGF, IGF, SCF and LIF in the absence feeder cells for 160 days (see 102 rejection above). Pain did not teach transfecting

the PGCs with a nucleic acid sequence encoding a protein functionally linked to regulatory sequences as claimed.

However, Han taught PGCs transfected in vitro expressing RSVLTR/beta-G2 plasmid.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to culture PGCs using the method of Pain and transfect the PGCs using the method of Han. One of ordinary skill in the art at the time the invention was made would have been motivated to transfect the PGCs of Pain with a retrovirus as taught by Han because the purpose of Pain was to develop avian cells that can be transfected (pg 2339, col. 1, first para.). One of ordinary skill in the art at the time the invention was made would have been motivated to transfect PGCs as taught by Han using the culture conditions of Pain to facilitate the proliferation of cells with an undifferentiated phenotype as suggested by Pain (pg 2345, col. 2, line 10).

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

Double Patenting

7. Claims 21-26, 30 and 31 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 and 10-12 of U.S. Patent No. 6,156,569, Dec. 5, 2000 for reasons of record. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-5 and 10-12 of '569 are obvious species of claims 21-28, 30 and 31 in the instant application. Claims 1-5 and 10-12

of '569 are directed toward a "pure population" of avian PGCs while the instant claims encompass any avian PGCs. The limitation of culturing the PGCs for at least 14 days in claim 1 of '569 is equivalent to claim 26 in the instant application. Applicants willingness to provide a terminal disclaimer upon allowance was provided in the response filed 2-19-02, paper number 12.

8. Claims 21-28, 30 and 31 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 and 10-12 of U.S. Patent No. 6,156,569, Dec. 5, 2000 in view of Pain (1996, Development, Vol. 122, pages 2239-2348) for reasons of record. The claims of '569 are directed toward culturing pure PGCs for at least 14 days. The claims do not recite the limitations of maintaining the cells for at least 25 days or 4 months. However, Pain taught culturing avian embryonic cells for at least 160 days (page 2345, col. 2). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the claimed invention in '569 to maintain the PGCs for at least 25 days or 4 months. One of ordinary skill would have been motivated to maintain the PGCs for at least 25 days or 4 months to increase the availability of the PGCs. Applicants willingness to provide a terminal disclaimer upon allowance was provided in the response filed 2-19-02, paper number 12.

9. Claims 21-32 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 and 10-12 of U.S. Patent No. 6,156,569, Dec. 5, 2000 in view of Pain (1996, Development, Vol. 122, pages 2239-2348) and Han et al.

(Asian-Australasian Journal of Animal Sciences, (1994) Vol. 7, No. 3, pg 427-434). The claims of '569 are directed toward culturing pure PGCs for at least 14 days. The claims do not recite the limitations of maintaining the cells for at least 25 days or 4 months or transfecting the PGCs with a nucleic acid encoding a protein operably linked to regulatory sequences. However, Pain taught culturing avian embryonic cells for at least 160 days (page 2345, col. 2) and Han taught transfecting PGCs in vitro with a nucleic acid sequence encoding a protein operably linked to regulatory sequences and obtaining expression of the protein. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the claimed invention in '569 to maintain the PGCs for at least 25 days or 4 months. One of ordinary skill would have been motivated to maintain the PGCs for at least 25 days or 4 months to increase the availability of the PGCs. One of ordinary skill in the art at the time the invention was made would have been motivated to transfect the PGCs with a retrovirus as taught by Han because the purpose of Pain was to develop avian cells that can be transfected (pg 2339, col. 1, first para.). One of ordinary skill in the art at the time the invention was made would have been motivated to transfect PGCs as taught by Han using the culture conditions of Pain to facilitate the proliferation of cells with an undifferentiated phenotype as suggested by Pain (pg 2345, col. 2, line 10).

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

10. Claims 21-32 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4, 5, 7, 8, 30, 31, 33-35,

37, 39, 40 and 43-46 of copending Application No. 09/127,624. Although the conflicting claims are not identical, they are not patentably distinct from each other because they both require culturing PGCs in media comprising LIF, bFGF, SCF and IGF for at least fourteen days.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-0120.

Questions of formal matters can be directed to the patent analyst, Dianiece Jacobs, who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-3388.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

The official fax number for this Group is (703) 308-4242.

Michael C. Wilson

MICHAEL WILSON
PRIMARY EXAMINER